WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, December 18, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L7	L6 and nt69l	1
☐	L6	neurotensin and bipolar	218
☐	L5	L4 and prepulse	2
☐	L4	L3 and NT69L	10
☐	L3	neurotensin agonist	32
	DB=DWPI,JPAB,EPAB,USOC,USPT,PGPB; PLUR=YES; OP=ADJ		
☐	L2	FEIFEL-DAVID!	2
☐	L1	FEIFEL-DAVID!	2

END OF SEARCH HISTORY

Case # 10/538,245-
WEST -
AD
12/18/06

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FILE 'BIOSIS' ENTERED AT 20:49:36 ON 18 DEC 2006
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FILE 'MEDLINE' ENTERED AT 20:49:36 ON 18 DEC 2006

=> s neurotensin agonist
L1          57 NEUROTENSIN AGONIST

=> s bipolar disorder
L2       30351 BIPOLAR DISORDER

=> s l1 and l2
L3           0 L1 AND L2

=> s pre-pulse inhibition
L4         145 PRE-PULSE INHIBITION

=> s l1 and l4
L5           0 L1 AND L4

=> s neurotensin
L6       10989 NEUROTENSIN

=> s l4 and l6
L7           1 L4 AND L6

=> disp l7 ibib abs 1-1

L7   ANSWER 1 OF 1  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
ACCESSION NUMBER:   2001:478140  BIOSIS
DOCUMENT NUMBER:    PREV200100478140
TITLE:              The role of neurotensin neurotransmission in the
                    effects of clozapine and risperidone on prepulse inhibition
                    in isolation reared rats.
AUTHOR(S):          Owens, M. J. [Reprint author]; Kinkead, B. [Reprint
                    author]; Egnatashvili, V. [Reprint author]; Cassell, T.
                    [Reprint author]; Nemeroff, C. B. [Reprint author]
CORPORATE SOURCE:   Psychiatry and Behav. Sci., Emory Univ., Atlanta, GA, USA
SOURCE:             Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1,
                    pp. 245. print.
                    Meeting Info.: 31st Annual Meeting of the Society for
                    Neuroscience. San Diego, California, USA. November 10-15,
                    2001.
                    ISSN: 0190-5295.
DOCUMENT TYPE:      Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 10 Oct 2001
                    Last Updated on STN: 23 Feb 2002
AB   There is strong evidence implicating the neurotensin (NT)
     neurotransmitter system in the mechanism of action of antipsychotic drugs.
     There are striking between the behavioral effects of centrally
     administered NT and peripherally administered antipsychotic drugs, leading
     to the hypothesis that NT may act as an endogenous antipsychotic.
     Although certain of these behavioral similarities may be unrelated to the
     antipsychotic potential of NT (e.g. hypothermia, analgesia), NT also
     resembles antipsychotic drugs in behavioral tests used to screen for
     antipsychotic activity.  One such test is pre-pulse
     inhibition (PPI) of the acoustic startle response.  Isolation
     rearing was used as a reliable means to disrupt PPI in rats.  Post-weaning
     social isolation of rats leads to disrupted PPI in the adult animal.  PPI
     deficits in isolation-reared animals are reversed by typical, as well as
     atypical, antipsychotic drugs.  Previously, we demonstrated that
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Case # 10/538245
STN ON LINE, BIOSIS
AD
12/18/06

pretreatment with the NT receptor antagonist SR142948A blocks restoration of isolation rearing-induced deficits in PPI by both haloperidol and quetiapine. In contrast, pretreatment with SR142948A did not block the restoration of isolation rearing-induced deficits in PPI by clozapine and risperidone. NT/NN mRNA and c-fos mRNA expression in the brains of treated and untreated isolation and socially reared rats are currently being measured in order to determine the critical difference between these antipsychotic drugs as it relates to NT neurotransmission. The results of these studies will provide valuable insight into the mechanism of action of antipsychotic drugs.

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FILE 'MEDLINE' ENTERED AT 20:56:23 ON 18 DEC 2006

FILE 'BIOSIS' ENTERED AT 20:56:23 ON 18 DEC 2006
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=> s sensorimotor gating
L9         1151 SENSORIMOTOR GATING

=> s neurotensin
L10       10989 NEUROTENSIN

=> s l9 and l10
L11          22 L9 AND L10

=> s l11 and pre-pulse inhibition
L12           0 L11 AND PRE-PULSE INHIBITION

=> disp l11 ibib abs 1-22
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FILE 'MEDLINE' ENTERED AT 21:11:45 ON 18 DEC 2006

FILE 'BIOSIS' ENTERED AT 21:11:45 ON 18 DEC 2006

=> s nt69l
L13 44 NT69L

=> s l13 and prepulse inhibition
L14 7 L13 AND PREPULSE INHIBITION

=> disp l14 ibib abs 1-7

L14 ANSWER 1 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2005010640 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15107967
TITLE: Neurotensin agonists block the prepulse inhibition deficits produced by a 5-HT2A and an alpha1 agonist.
AUTHOR: Shilling P D; Melendez G; Priebe K; Richelson E; Feifel D
CORPORATE SOURCE: Department of Psychiatry, University of California San Diego, La Jolla, CA 92093, USA.
CONTRACT NUMBER: MH27692 (NIMH)
MH62451 (NIMH)
SOURCE: Psychopharmacology, (2004 Sep) Vol. 175, No. 3, pp. 353-9. Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 8 Jan 2005
Last Updated on STN: 3 Feb 2005
Entered Medline: 2 Feb 2005

AB RATIONALE: Neurotensin (NT) agonists have been proposed as potential antipsychotics based exclusively upon their ability to inhibit dopamine-2 (D2) receptor transmission. Several other pharmacological mechanisms have been implicated in enhancing the antipsychotic profile produced by D2 inhibition alone. These include inhibition of 5-HT2A and alpha1-adrenoceptors. Recently, we reported that systemic administration of the neurotensin agonist PD149163 blocks deficits in prepulse inhibition (PPI) of the startle reflex produced by the 5-HT2A receptor agonist DOI. This suggested that NT agonists could inhibit 5-HT2A modulation of neurotransmission. OBJECTIVE: To determine if other peripherally administered NT agonists shared this effect, we examined the effects of NT69L, another NT agonist, on DOI-induced PPI deficits. In addition, to determine if NT agonists also inhibit alpha1-adrenoceptor neurotransmission, we examined the effects of PD149163 and NT69L on PPI deficits induced by the alpha1-adrenoceptor agonist, cirazoline. METHODS: In the NT69L/DOI study, rats received subcutaneous (SC) injections of NT69L (0, 0.1, 1, or 2 mg/kg) followed 30 min later by SC saline or DOI (0.5 mg/kg). In the NT agonist/cirazoline studies, animals received SC injections of either PD149163 (0, 0.01, 0.1, or 1 mg/kg) or NT69L (0, 0.01, 0.1, or 1 mg/kg) followed 30 min later by SC saline or cirazoline (0.7 mg/kg). Animals were tested in startle chambers 20 min later. RESULTS: In all three experiments the PPI disruption produced by DOI and cirazoline was blocked by the NT agonists. CONCLUSIONS: These findings provide strong evidence that NT agonists inhibit 5-HT2A and alpha1-adrenoceptor modulation of neurotransmission, pharmacological effects that, in conjunction with their known inhibition of dopamine transmission, strengthen the antipsychotic potential of NT agonists.

L14 ANSWER 2 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003313851 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12842291
TITLE: The effects of systemic NT69L, a neurotensin agonist, on baseline and drug-disrupted prepulse inhibition.
AUTHOR: Shilling P D; Richelson E; Feifel D
CORPORATE SOURCE: Department of Psychiatry, University of California, San Diego, La Jolla, CA 92093, USA.
CONTRACT NUMBER: 5T32 MH18399 (NIMH)
MH27692 (NIMH)
MH62451 (NIMH)

SOURCE: Behavioural brain research, (2003 Jul 14) Vol. 143, No. 1, pp. 7-14.
Journal code: 8004872. ISSN: 0166-4328.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 8 Jul 2003
Last Updated on STN: 10 Sep 2003
Entered Medline: 9 Sep 2003

AB Centrally administered neurotensin (NT) produces behavioral and biochemical effects that are very similar to the effects of antipsychotic drugs. Therefore, there is much interest in the potential use of NT agonists as antipsychotic drugs. We have previously reported that PD149163, a NT(8-13) analogue, produced effects on prepulse inhibition (PPI) of startle after systemic administration that were suggestive of an atypical antipsychotic-like drug profile. To determine if these effects are shared by other peripherally administered NT agonists, we tested the effects of NT69L, a recently developed NT agonist that penetrates the CNS, on drug-induced PPI deficits. In the first experiment, rats received subcutaneous (s.c.) injections of NT69L (vehicle, 0.08, 0.25, and 1.0mg/kg) followed 30min later by subcutaneous saline or D-amphetamine (2.0mg/kg). In the second experiment, NT69L injections were followed by saline or the non-competitive NMDA antagonist dizocilpine (0.1mg/kg). Both D-amphetamine and dizocilpine significantly decreased PPI as expected. In the first experiment, NT69L significantly increased PPI levels at baseline and after D-amphetamine. In the second experiment, NT69L attenuated PPI deficits produced by dizocilpine, without increasing baseline PPI. In addition, NT69L had no effect on startle magnitude. The effects of NT69L in these studies were similar in some ways to the effects of PD149163 and were also consistent with the preclinical effects of atypical antipsychotic drugs. These data provide further support for the notion that NT agonists may have use as novel antipsychotic drugs. Furthermore, the ability of NT69L and PD149163 to attenuate dizocilpine-disrupted PPI, an antipsychotic drug effect not mediated by dopamine, suggests that NT agonists may produce some of their antipsychotic-like effects by modulating neurotransmitter systems other than dopamine, such as serotonin, noradrenaline or glutamate.

L14 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:29705 BIOSIS
DOCUMENT NUMBER: PREV200500028581
TITLE: Neurotensin agonists block the prepulse inhibition deficits produced by a 5-HT2A and an alpha1 agonist.
AUTHOR(S): Shilling, P. D.; Melendez, G.; Priebe, K.; Richelson, E.; Feifel, D. [Reprint Author]
CORPORATE SOURCE: Dept Psychiat, Univ Calif San Diego, La Jolla, CA, 92093, USA
dfeifel@ucsd.edu
SOURCE: Psychopharmacology, (September 2004) Vol. 175, No. 3, pp. 353-359. print.
ISSN: 0033-3158 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2005
Last Updated on STN: 5 Jan 2005

AB Rationale: Neurotensin (NT) agonists have been proposed as potential antipsychotics based exclusively upon their ability to inhibit dopamine-2 (D2) receptor transmission. Several other pharmacological mechanisms have been implicated in enhancing the antipsychotic profile produced by D2

inhibition alone. These include inhibition of 5-HT2A and alpha1-adrenoceptors. Recently, we reported that systemic administration of the neurotensin agonist PD149163 blocks deficits in prepulse inhibition (PPI) of the startle reflex produced by the 5-HT2A receptor agonist DOI. This suggested that NT agonists could inhibit 5-HT2A modulation of neurotransmission. Objective: To determine if other peripherally administered NT agonists shared this effect, we examined the effects of NT69L, another NT agonist, on DOI-induced PPI deficits. In addition, to determine if NT agonists also inhibit alpha1-adrenoceptor neurotransmission, we examined the effects of PD149163 and NT69L on PPI deficits induced by the alpha1-adrenoceptor agonist, cirazoline. Methods: In the NT69L/DOI study, rats received subcutaneous (SC) injections of NT69L (0, 0.1, 1, or 2 mg/kg) followed 30 min later by SC saline or DOI (0.5 mg/kg). In the NT agonist/cirazoline studies, animals received SC injections of either PD149163 (0, 0.01, 0.1, or 1 mg/kg) or NT69L (0, 0.0 1, 0.1, or 1 mg/kg) followed 30 min later by SC saline cirazoline (0.7 mg/kg). Animals were tested in startle chambers 20 min later. Results: In all three experiments the PPI disruption produced by DOI and cirazoline was blocked by the NT agonists. Conclusions: These findings provide strong evidence that NT agonists inhibit 5-HT2A and alpha1-adrenoceptor modulation of neurotransmission, pharmacological effects that, in conjunction with their known inhibition of dopamine transmission, strengthen the antipsychotic potential of NT agonists.

L14 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:204806 BIOSIS
DOCUMENT NUMBER: PREV200400205347
TITLE: Neurotensin agonist, NT69L, induces regional c - Fos expression in rat brain with a pattern similar to atypical antipsychotics.
AUTHOR(S): Ambrose, C. [Reprint Author]; Button, D. [Reprint Author]; Richelson, E.; Novakovic, S. D. [Reprint Author]
CORPORATE SOURCE: CNS Pharmacol., Roche Palo Alto, LLC, Palo Alto, CA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 847.17. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB Many stimuli such as stress or antipsychotic drugs elicit brain region-specific induction of the immediate-early gene, c-fos. As a marker of neuronal activation c-fos expression provides important functional and anatomical information. In rat brain, the region-specific c-fos expression is activated differently by antipsychotics exhibiting distinct clinical profiles. Typical antipsychotics induce c-fos predominately in striatum, a response correlated with extrapyramidal side effects. Atypical antipsychotics elicit minimal c-fos induction in striatum but significant c-fos induction is found in the prefrontal cortex and limbic structures. Both typical and atypical antipsychotics activate neurons in the nucleus accumbens. Defective neurotensin (NT) regulation of dopaminergic systems is implicated in schizophrenia and NT agonists have efficacy in prepulse inhibition of startle, an animal model of sensorimotor gating strongly predictive for antipsychotic activity. We compared the patterns of c-fos induction for several antipsychotic drugs with that of NT agonist peptide, NT69L. Male Sprague Dawley rats were given vehicle or drug (i.p.) 2 hours prior to brain dissection. Brains were embedded in a gelatin matrix, cryo-sectioned and stained with anti-c-fos antibodies. C-fos

immunoreactive neurons in various brain regions were counted using Simple PCI imaging software. In addition to NT69L, atypical drugs olanzapine, clozapine, risperidone and typicals, haloperidol and fluphenazine were tested. Similar to clozapine, NT69L (1 mg/kg) exhibited minimal c-fos induction in the striatum, with elevated c-fos in the nucleus accumbens shell, posterior olfactory nucleus, cingulate cortex and significant elevation in the paraventricular nucleus in the hypothalamus. NT69L also elevated c-fos levels in the area postrema and solitary tract.

L14 ANSWER 5 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:204797 BIOSIS
DOCUMENT NUMBER: PREV200400205338
TITLE: NT69L, a neurotensin agonist, exhibits antipsychotic - like effects in the prepulse inhibition paradigm.
AUTHOR(S): Shilling, P. D. [Reprint Author]; Melendez, G. [Reprint Author]; Richelson, E.; Feifel, D. [Reprint Author]
CORPORATE SOURCE: Psychiatry, Univ. of California,San Diego, La Jolla, CA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 847.8. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB Central administration of neurotensin (NT) produces biochemical and behavioral effects that are similar to the effects of antipsychotic drugs. We previously reported that systemic administration of PD149163, a NT(8-13) analog, produced atypical antipsychotic-like effects on prepulse inhibition (PPI). To determine if other systemically administered NT agonists share these effects, we investigated the effects of NT69L, a new NT agonist that penetrates the blood-brain-barrier, on drug-induced PPI deficits. In one experiment, rats received subcutaneous (SC) NT69L injections (saline, 0.08, 0.25, 1.0 mg/kg) followed 30 min later by SC saline or D-amphetamine (2.0 mg/kg). In a second experiment, NT69L injections were followed by saline or the non-competitive NMDA antagonist dizocilpine (DIZ) (0.1 mg/kg). Since NT69L attenuated DIZ-induced PPI deficits, an effect produced by drugs that block serotonin (5HT)2A and alpha-1 transmission, we also tested the effects of NT69L on PPI disruption produced by 2,5-dimethoxy-4-iodoamphetamine (DOI) (0.5 mg/kg), a direct 5HT2A agonist and cirazoline, an alpha-1 agonist. Similar to the effects of PD149163, NT69L significantly antagonized the PPI deficits produced by all compounds tested. These results are consistent with the notion that NT agonists may have use as novel antipsychotic drugs. The ability of NT69L and PD149163 to block DIZ-disrupted PPI, an antipsychotic drug effect not mediated by dopamine, suggests that NT agonists may produce some of their antipsychotic-like effects by modulating other neurotransmitter systems. The effects of NT69L on DOI-and cirazoline-induced PPI disruption suggest that the effects of NT agonists on DIZ-induced PPI deficits could be mediated through 5HT and/or noradrenergic neurotransmission. These effects have not been previously associated with antipsychotic-like NT activity.

L14 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:442868 BIOSIS
DOCUMENT NUMBER: PREV200300442868
TITLE: The effects of systemic NT69L, a neurotensin

agonist, on baseline and drug-disrupted prepulse inhibition.
AUTHOR(S): Shilling, P. D.; Richelson, E.; Feifel, D. [Reprint Author]
CORPORATE SOURCE: Department of Psychiatry, University of California, San Diego, La Jolla, CA, 92093, USA
dfeifel@ucsd.edu
SOURCE: Behavioural Brain Research, (14 July 2003) Vol. 143, No. 1, pp. 7-14. print.
CODEN: BBREDI. ISSN: 0166-4328.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Sep 2003
Last Updated on STN: 24 Sep 2003

AB Centrally administered neurotensin (NT) produces behavioral and biochemical effects that are very similar to the effects of antipsychotic drugs. Therefore, there is much interest in the potential use of NT agonists as antipsychotic drugs. We have previously reported that PD149163, a NT(8-13) analogue, produced effects on prepulse inhibition (PPI) of startle after systemic administration that were suggestive of an atypical antipsychotic-like drug profile. To determine if these effects are shared by other peripherally administered NT agonists, we tested the effects of NT69L, a recently developed NT agonist that penetrates the CNS, on drug-induced PPI deficits. In the first experiment, rats received subcutaneous (s.c.) injections of NT69L (vehicle, 0.08, 0.25, and 1.0 mg/kg) followed 30 min later by subcutaneous saline or D-amphetamine (2.0 mg/kg). In the second experiment, NT69L injections were followed by saline or the non-competitive NMDA antagonist dizocilpine (0.1 mg/kg). Both D-amphetamine and dizocilpine significantly decreased PPI as expected. In the first experiment, NT69L significantly increased PPI levels at baseline and after D-amphetamine. In the second experiment, NT69L attenuated PPI deficits produced by dizocilpine, without increasing baseline PPI. In addition, NT69L had no effect on startle magnitude. The effects of NT69L in these studies were similar in some ways to the effects of PD149163 and were also consistent with the preclinical effects of atypical antipsychotic drugs. These data provide further support for the notion that NT agonists may have use as novel antipsychotic drugs. Furthermore, the ability of NT69L and PD149163 to attenuate dizocilpine-disrupted PPI, an antipsychotic drug effect not mediated by dopamine, suggests that NT agonists may produce some of their antipsychotic-like effects by modulating neurotransmitter systems other than dopamine, such as serotonin, noradrenaline or glutamate.

L14 ANSWER 7 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:267832 BIOSIS
DOCUMENT NUMBER: PREV200300267832
TITLE: THE NEUROTENSIN AGONIST NT69L REVERSES DIZOCILPINE - INDUCED DISRUPTION OF PREPULSE INHIBITION IN THE RAT.
AUTHOR(S): Hedley, L. R. [Reprint Author]; Secchi, R. [Reprint Author]; Bingham, S. [Reprint Author]; Sung, E. [Reprint Author]; Richelson, E.; Button, D.
CORPORATE SOURCE: Neurobehavior, Pharmacology, Roche Bioscience, Palo Alto, CA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 9.5. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB The endogenous tridecapeptide neurotensin (NT) possesses antipsychotic properties in animal models. The NT mimetic PD149163 reversed the disruptive effects of the dopamine releaser amphetamine and the glutamate antagonist dizocilpine on prepulse inhibition (PPI) of the acoustic startle response in rats (Feifel et al., JPET 288: 710-713, 1999); a sensorimotor gating model for schizophrenia. PPI refers to the phenomenon that a non-startle eliciting stimulus (prepulse) presented before a startling stimulus (pulse) activates an inhibitory process that attenuates (gates) the startle response. Herein, we assessed the antipsychotic properties of the NT agonist NT69L in the rat PPI model and the mouse apomorphine climbing test. In addition, the combination of SR142948A and NT69L was evaluated in measurements of core body temperature in mice and rats. NT69L reversed the effects of dizocilpine on PPI (MED ltoreq 0.3mg/kg, i.p.) and apomorphine-induced climbing (MED = 3 mg/kg, i.p.). NT69L did not induce catalepsy or any other side effects. NT69L induced a dose dependant hypothermic effect in both rats and mice. The hypothermic effect of NT69L (1 mg/kg, i.p.) was reversed by the NT antagonist SR142948A (0.1 mg/kg, i.p.) in the rat, thus suggesting that its behavioral effects involve activation of NT receptors. Taken together, the activity of NT69L in two models for schizophrenia and the lack of behavioral side effects, suggests that NT agonists may represent a novel class of antipsychotics.

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ANSWER 17 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:472156 BIOSIS
DOCUMENT NUMBER: PREV200100472156
TITLE: Prepulse inhibition of the acoustic startle response in neurotensin knock-out mice.
AUTHOR(S): Kinkead, B. [Reprint author]; Cassell, T. [Reprint author]; Owens, M. J. [Reprint author]; Dobner, P. R.; Deitemeyer, N.; Nemeroff, C. B. [Reprint author]
CORPORATE SOURCE: Psychiatry Behav. Sci., Emory Univ. Sch. Med., Atlanta, GA, USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 245. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Oct 2001
Last Updated on STN: 23 Feb 2002

AB There is increasing evidence that a deficit in sensorimotor gating is a cardinal feature of the underlying pathophysiology of schizophrenia. The hypothesized deficit in gating or internal screening of sensory input in schizophrenic patients is viewed as leading to an involuntary flooding of indifferent sensory data, likely contributing to the cognitive fragmentation and thought disorder characteristic of this disease. One model of sensorimotor gating commonly used to assess these deficits is prepulse inhibition (PPI) of the acoustic startle reflex. PPI is generally acknowledged to be a measure of preattentive sensorimotor gating. In humans, PPI has repeatedly and consistently been shown to be disrupted in schizophrenic patients and patients with high schizotypal scores. In rats, indirect dopamine agonists, NMDA antagonists, isolation rearing or hippocampal lesions disrupt PPI. These disruptions are restored by typical and atypical antipsychotic drugs, but not by treatment with antidepressant or anxiolytic drugs. There is strong evidence implicating the neurotensin (NT) system in the pathophysiology of schizophrenia and NT has been hypothesized to be an endogenous antipsychotic. In order to examine the role of the NT system in the regulation of PPI, NT knockout mice were tested in the PPI paradigm. Preliminary results indicate that both NT -/- and NT +/- mice have significantly disrupted PPI compared to NT +/+ mice. These results will provide significant insight into the role of the NT system in sensorimotor gating and the pathophysiology of schizophrenia.

ANSWER 15 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:267832 BIOSIS
DOCUMENT NUMBER: PREV200300267832
TITLE: THE NEUROTENSIN AGONIST NT69L REVERSES DIZOCILPINE - INDUCED DISRUPTION OF PREPULSE INHIBITION IN THE RAT.
AUTHOR(S): Hedley, L. R. [Reprint Author]; Secchi, R. [Reprint Author]; Bingham, S. [Reprint Author]; Sung, E. [Reprint Author]; Richelson, E.; Button, D.
CORPORATE SOURCE: Neurobehavior, Pharmacology, Roche Bioscience, Palo Alto, CA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 9.5. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB The endogenous tridecapeptide neurotensin (NT) possesses antipsychotic properties in animal models. The NT mimetic PD149163 reversed the disruptive effects of the dopamine releaser amphetamine and the glutamate antagonist dizocilpine on prepulse inhibition (PPI) of the acoustic startle response in rats (Feifel et al., JPET 288: 710-713, 1999); a sensorimotor gating model for schizophrenia.
PPI refers to the phenomenon that a non-startle eliciting stimulus (prepulse) presented before a startling stimulus (pulse) activates an inhibitory process that attenuates (gates) the startle response. Herein, we assessed the antipsychotic properties of the NT agonist NT69L in the rat PPI model and the mouse apomorphine climbing test. In addition, the combination of SR142948A and NT69L was evaluated in measurements of core body temperature in mice and rats. NT69L reversed the effects of dizocilpine on PPI (MED ltoreq 0.3mg/kg, i.p.) and apomorphine-induced climbing (MED = 3 mg/kg, i.p.). NT69L did not induce catalepsy or any other side effects. NT69L induced a dose dependant hypothermic effect in both rats and mice. The hypothermic effect of NT69L (1 mg/kg, i.p.) was reversed by the NT antagonist SR142948A (0.1 mg/kg, i.p.) in the rat, thus suggesting that its behavioral effects involve activation of NT receptors. Taken together, the activity of NT69L in two models for schizophrenia and the lack of behavioral side effects, suggests that NT agonists may represent a novel class of antipsychotics.

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FILE LAST UPDATED: 17 Dec 2006  (20061217/ED)

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E2            1     FEIFEI CHEN/IN
E3            1 --> FEIFEL DAVID/IN
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E5            4     FEIFEL KLAUS/IN
E6            1     FEIFEL KLAUS HELMUT/IN
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E13           1     FEIG JAMES E/IN
E14           1     FEIG JONATHAN/IN
E15           1     FEIG PETER/IN
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E19           2     FEIGE ALBRECHT/IN
E20           6     FEIGE ANDRE/IN
E21           2     FEIGE CHRISTIAN/IN
E22           1     FEIGE CHRISTINA/IN
E23           1     FEIGE DIETER/IN
E24           1     FEIGE DIETER K/IN
E25           1     FEIGE EKKEHARD/IN

=> S (E3) AND (NEUROTENSIN)
             1 "FEIFEL DAVID"/IN
          4822 NEUROTENSIN
            27 NEUROTENSINS
          4825 NEUROTENSIN
                 (NEUROTENSIN OR NEUROTENSINS)
L1           1 ("FEIFEL DAVID"/IN) AND (NEUROTENSIN)

=> DIS L1 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.74 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y
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L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:515667 CAPLUS
DOCUMENT NUMBER: 141:65121
TITLE: Method of inhibiting neural transmission mediated by serotonin 2a receptors and enhancing sensorimotor gating, methods for identifying psychotropic agents, and animal models
INVENTOR(S): Feifel, David
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004053093	A2	20040624	WO 2003-US39196		20031208
WO 2004053093	A3	20050728			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003296422	A1	20040630	AU 2003-296422		20031208
US 2006179492	A1	20060810	US 2005-538245		20050607
PRIORITY APPLN. INFO.:			US 2002-431937P	P	20021209
			WO 2003-US39196	W	20031208

ABSTRACT:
Methods are disclosed for treating neuropsychiatric disorders and disorders associated with sensorimotor gating deficits and/or prepulse inhibition disorders and improving sensorimotor gating in normal subjects. Also provided are animal models useful for identifying agents that modulate sensorimotor gating activity for preclin. testing of psychotropic drugs.

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